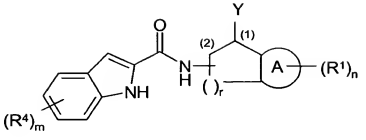
Claims

1. A compound of formula (1):



(1)

wherein:

A is phenylene or heteroarylene;

n is 0, 1, or 2;

m is 0, 1, or 2;

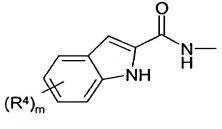
R^1 is independently selected from halo, nitro, cyano, hydroxy, carboxy, carbamoyl, *N*-C_{1-4}alkylcarbamoyl, *N*,*N*-(C_{1-4}alkyl)$_2$carbamoyl, sulphamoyl, *N*-C_{1-4}alkylsulphamoyl, *N*,*N*-(C_{1-4}alkyl)$_2$sulphamoyl, -S(O)$_b$$C_{1-4}$alkyl (wherein b is 0,1, or 2), C_{1-4}alkyl, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{1-4}alkoxy, C_{1-4}alkanoyl, C_{1-4}alkanoyloxy, hydroxyC_{1-4}alkyl, fluoromethyl, difluoromethyl, trifluoromethyl, and trifluoromethoxy; or

when n is 2, the two R^1 groups, together with the carbon atoms of A to which they are attached, may form a 4- to 7-membered ring, optionally containing 1 or 2 heteroatoms independently selected from O, S, and N, and optionally being substituted with one or two methyl groups;

R^4 is independently selected from hydrogen, halo, nitro, cyano, hydroxy, fluoromethyl, difluoromethyl, trifluoromethyl, trifluoromethoxy, carboxy, carbamoyl, C_{1-4}alkyl, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{1-4}alkoxy, and C_{1-4}alkanoyl;

r is 1 or 2;

when r is 1 the group

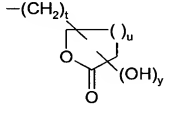


is a substituent on carbon (2);

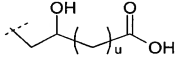
when r is 2 (thereby forming a six membered ring) the same group is a substituent on carbon (2) or on carbon (3);

Y is $-NR^2R^3$ or $-OR^3$;

R^2 and R^3 are independently selected from hydrogen, hydroxy, C_{1-4}alkoxy, C_{1-4}alkanoyl, carbamoyl, C_{3-7}cycloalkyl (optionally substituted with 1 or 2 hydroxy groups), cyano(C_{1-4})alkyl, heterocyclyl, aryl, C_{1-4}alkyl [optionally substituted with 1 or 2 R^8 groups], $-COR^8$, $-SO_bR^8$ (wherein b is 0, 1, or 2), and groups of the formulae B and B'



(B)



(B')

wherein y is 0 or 1, t is 0, 1, 2, or 3 and u is 1 or 2; provided that the hydroxy group is not a substituent on the ring carbon adjacent to the ring oxygen; or

wherein NR^2R^3 may form a 4- to 7-membered saturated, partially saturated, or unsaturated ring, optionally containing 1, 2, or 3 additional heteroatoms independently selected from N, O, and S, wherein any $-CH_2-$ may optionally be replaced by –C(=O)-, and any N or S atom may optionally be oxidized to form an N-oxide, SO, or SO_2 group respectively, and wherein the ring is optionally substituted with 1 or 2 substituents independently selected from halo, cyano, C_{1-4}alkyl, hydroxy, C_{1-4}alkoxy, and C_{1-4}alkyl$S(O)_b$- (wherein b is 0, 1, or 2);

R^8 is independently selected from hydrogen, hydroxy, C_{1-4}alkyl, C_{2-4}alkenyl, C_{1-4}alkoxy, cyano(C_{1-4})alkyl, amino(C_{1-4})alkyl [optionally substituted on nitrogen with 1 or 2 groups selected from C_{1-4}alkyl, hydroxy, hydroxy(C_{1-4})alkyl, dihydroxy(C_{1-4})alkyl, $-CO_2C_{1-4}$alkyl, aryl, and aryl(C_{1-4})alkyl], halo(C_{1-4})alkyl, dihalo(C_{1-4})alkyl, trihalo(C_{1-4})alkyl, hydroxy(C_{1-4})alkyl, dihydroxy(C_{1-4})alkyl, C_{1-4}alkoxyC_{1-4}alkoxy, C_{1-4}alkoxyC_{1-4}alkyl, hydroxyC_{1-4}alkoxy, 5- and 6-membered cyclic acetals and mono- and di-methyl derivatives thereof, aryl, heterocyclyl, (heterocyclyl)C_{1-4}alkyl, C_{3-7}cycloalkyl (optionally substituted with 1 or 2 hydroxy groups,

C_{1-4}alkyl, or -C(O)OC_{1-4}alkyl), C_{1-4}alkanoyl, C_{1-4}alkylS(O)$_b$- (wherein b is 0, 1, or 2), C_{3-6}cycloalkylS(O)$_b$- (wherein b is 0, 1, or 2), arylS(O)$_b$- (wherein b is 0, 1, or 2), heterocyclylS(O)$_b$- (wherein b is 0, 1, or 2), benzylS(O)$_b$- (wherein b is 0, 1, or 2), C_{1-4}alkylS(O)$_c$(C_{1-4})alkyl (wherein c is 0, 1, or 2), -N(OH)CHO, -C(=N-OH)NH_2, -C(=N-OH)NHC_{1-4}alkyl, -C(=N-OH)N(C_{1-4}alkyl)$_2$, -C(=N-OH)NHC_{3-6}cycloalkyl, -C(=N-OH)N(C_{3-6}cycloalkyl)$_2$, -COCOOR^9, -C(O)N(R^9)(R^{10}), -NHC(O)R^9, -C(O)NHSO_2(C_{1-4}alkyl), -NHSO_2R^9, (R^9)(R^{10})NSO_2-, -COCH_2OR^{11}, (R^9)(R^{10})N-, -COOR^9, -CH_2OR^9, –CH_2COOR^9, –CH_2OCOR^9, -CH_2CH(CO_2R^9)OH, –CH_2C(O)NR^{9}R^{10}, -(CH_2)$_w$CH(NR^{9}R^{10})CO_2R$^{9'}$ (wherein w is 1, 2 or 3), and -(CH_2)$_w$CH(NR^{9}R^{10})CO(NR$^{9'}$R$^{10'}$) (wherein w is 1, 2, or 3) ;

R^9, R$^{9'}$, R^{10}, and R$^{10'}$ are independently selected from hydrogen, hydroxy, C_{1-4}alkyl (optionally substituted with 1 or 2 R^{13}), C_{2-4}alkenyl, C_{3-7}cycloalkyl (optionally substituted with 1 or 2 hydroxy groups), cyano(C_{1-4})alkyl, trihaloalkyl, aryl, heterocyclyl, heterocyclyl(C_{1-4}alkyl), and -C(=O)O(C_{1-4})alkyl; or

R^9 and R^{10} together with the nitrogen to which they are attached, or R$^{9'}$ and R$^{10'}$ together with the nitrogen to which they are attached, form a 4- to 6-membered ring where the ring is optionally substituted on carbon with 1 or 2 substituents independently selected from oxo, hydroxy, carboxy, halo, nitro, cyano, carbonyl, C_{1-4}alkoxy, and heterocyclyl; or the ring may be optionally substituted on two adjacent carbons with –O-CH_2-O- to form a cyclic acetal wherein one or both of the hydrogens of the -O-CH_2-O- group may be replaced by a methyl;

R^{13} is selected from halo, trihalomethyl, and C_{1-4}alkoxy; and

R^{11} is independently selected from hydrogen, C_{1-4}alkyl, and hydroxyC_{1-4}alkyl; or a pharmaceutically acceptable salt or prodrug thereof.

2. A compound of claim 1, wherein:

R^2 and R^3 are independently selected from hydrogen, hydroxy, C_{1-4}alkyl [optionally substituted with 1 or 2 R^8 groups], C_{3-7}cycloalkyl (optionally substituted with 1 or 2 hydroxy groups), cyano(C_{1-4})alkyl, phenyl, morpholino, morpholinyl, piperidino, piperidyl, pyridyl, pyranyl, pyrrolyl, imidazolyl, thiazolyl, thienyl, thiadiazolyl, piperazinyl, isothiazolidinyl, 1,3,4-triazolyl, tetrazolyl, pyrrolidinyl, thiomorpholino, pyrrolinyl, homopiperazinyl, 3,5-dioxapiperidinyl, pyrimidyl, pyrazinyl, pyridazinyl, pyrazolyl, pyrazolinyl, isoxazolyl, 4-oxopydridyl, 2-oxopyrrolidyl, 4-oxothiazolidyl, furyl, thienyl, oxazolyl, 1,3,4-oxadiazolyl, and 1,2,4-oxadiazolyl,

tetrahydrothiopyranyl, 1-oxotetrahydrothiopyranyl, 1,1-dioxotetrahydrothiopyranyl, -COR^8, and $-SO_bR^8$ (wherein b is 0, 1, or 2);

R^8 is independently selected from hydrogen, hydroxy, C_{1-4}alkoxy, C_{1-4}alkoxyC_{1-4}alkyl, C_{1-4}alkoxyC_{1-4}alkoxy, hydroxyC_{1-4}alkoxy, C_{1-4}alkyl, , amino(C_{1-4})alkyl [optionally substituted on nitrogen with 1 or 2 groups selected from C_{1-4}alkyl, hydroxy(C_{1-4})alkyl, dihydroxy(C_{1-4})alkyl, -CO_2C_{1-4}alkyl, aryl, and aryl(C_{1-4})alkyl], C_{2-4}alkenyl, C_{3-7}cycloalkyl (optionally substituted with -C(O)OC_{1-4}alkyl), 5- and 6-membered cyclic acetals and mono- and di-methyl derivatives thereof, halo(C_{1-4})alkyl, dihalo(C_{1-4})alkyl, trihalo(C_{1-4})alkyl, hydroxy(C_{1-4})alkyl, dihydroxy(C_{1-4})alkyl, cyano(C_{1-4})alkyl, heterocyclyl, heterocyclylC_{1-4}alkyl, aryl, C_{1-4}alkyl$S(O)_b$- (wherein b is 0, 1, or 2), C_{3-6}cycloalkyl$S(O)_b$- (wherein b is 0, 1, or 2), aryl$S(O)_b$- (wherein b is 0, 1, or 2), heterocyclyl$S(O)_b$- (wherein b is 0, 1, or 2), benzyl$S(O)_b$- (wherein b is 0, 1, or 2), C_{1-4}alkyl$S(O)_c(C_{1-4})$alkyl (wherein c is 0, 1, or 2), -$CH_2CH(NR^9R^{10})CO(NR^{9'}R^{10'})$, -$CH_2OR^9$, $(R^9)(R^{10})N$-, $-COOR^9$, $-CH_2COOR^9$, -$C(O)N(R^9)(R^{10})$, -$CH_2CH(CO_2R^9)OH$, $-H_2CONR^9R^{10}$, -$CH_2CH(NR^9R^{10})CO_2R^{9'}$, and $-CH_2OCOR^9$;

R^9, $R^{9'}$, R^{10}, and $R^{10'}$ are independently selected from hydrogen, C_{1-4}alkyl (optionally substituted with 1 or 2 R^{13}), C_{3-7}cycloalkyl (optionally substituted with 1 or 2 hydroxy groups), -C(=O)O^{t}Bu, C_{2-4}alkenyl, cyano(C_{1-4})alkyl, phenyl (optionally substituted with 1 or 2 groups selected from nitro, halo, hydroxy, and cyano); or

R^9 and R^{10} together with the nitrogen to which they are attached, or $R^{9'}$ and $R^{10'}$ together with the nitrogen to which they are attached, form a 4- to 6-membered ring where the ring is optionally substituted on carbon with 1 or 2 substituents independently selected from oxo, hydroxy, carboxy, halo, nitro, cyano, carbonyl, and C_{1-4}alkoxy; or the ring may be optionally substituted on two adjacent carbons with $-O-CH_2-O-$ to form a cyclic acetal wherein one or both of the hydrogens of the $-O-CH_2-O-$ group may be replaced by a methyl; and

R^{13} is selected from halo, trihalomethyl, and C_{1-4}alkoxy;

or a pharmaceutically acceptable salt or an in-vivo hydrolysable ester thereof.

3. A compound of claim 1, wherein:

R^2 and R^3 are independently selected from hydrogen, C_{1-4}alkyl [optionally substituted with 1 or 2 R^8 groups], -COR^8 and $-SO_bR^8$ (wherein b is 0, 1, or 2);

R^8 is independently selected from hydrogen, hydroxy, C_{1-4}alkoxy, C_{1-4}alkoxyC_{1-4}alkyl, C_{1-4}alkyl, amino(C_{1-4})alkyl [optionally substituted on nitrogen with 1 or 2 groups selected from C_{1-4}alkyl, hydroxy(C_{1-4})alkyl, dihydroxy(C_{1-4})alkyl, -CO_2C_{1-4}alkyl, phenyl, and aryl(C_{1-4})alkyl], C_{2-4}alkenyl, C_{3-7}cycloalkyl (optionally substituted with -C(O)OC_{1-4}alkyl), 5- and 6-membered cyclic acetals and mono- and di-methyl derivatives thereof, halo(C_{1-4})alkyl, trihalo(C_{1-4})alkyl, hydroxy(C_{1-4})alkyl, dihydroxy(C_{1-4})alkyl, cyano(C_{1-4})alkyl, furyl (optionally substituted on carbon with 1 or 2 nitro groups), thienyl (optionally substituted on carbon with 1 or 2 nitro groups), morpholino, furyl(C_{1-4})alkyl (wherein furyl is optionally substituted on carbon with 1 or 2 nitro groups), thienyl(C_{1-4})alkyl (wherein thienyl is optionally substituted on carbon by 1 or 2 nitro groups), 1,2,4-oxadiazolyl, tetrazolyl, imidazolyl, pyrrolidinyl, piperidyl, pyridyl, tetrahydrofuryl, tetrahydropyranyl, 1-oxo-tetrahydrothiopyranyl, tetrahydrothienyl, phenyl (optionally substituted with 1 or 2 groups selected from nitro, halo, cyano, hydroxy, and C_{1-4}alkyl), pyrazinyl, piperazinyl, 4-methylpiperazino, C_{1-4}alkyl$S(O)_b$- (wherein b is 0, 1, or 2), C_{3-6}cycloalkyl$S(O)_b$- (wherein b is 0, 1, or 2), aryl$S(O)_b$- (wherein b is 0, 1, or 2), heterocyclyl$S(O)_b$- (wherein b is 0, 1, or 2), -$CH_2CH(NR^9R^{10})CO(NR^{9'}R^{10'})$, -$CH_2OR^9$, $(R^9)(R^{10})N$-, -$COOR^9$, -CH_2COOR^9, -$C(O)N(R^9)(R^{10})$, -$CH_2CH(CO_2R^9)OH$, -$CH_2CONR^9R^{10}$, -$CH_2CH(NR^9R^{10})CO_2R^{9'}$, and -$CH_2OCOR^9$; and

R^9, $R^{9'}$, R^{10}, and $R^{10'}$ are independently selected from hydrogen, C_{1-4}alkyl (optionally substituted with 1 or 2 hydroxy groups), C_{2-4}alkenyl, and phenyl (optionally substituted with 1 or 2 groups selected from nitro, halo, hydroxy, and cyano);

or a pharmaceutically acceptable salt or an in-vivo hydrolysable ester thereof.

4. A compound of claim 1, wherein Y is NR^2R^3, or a pharmaceutically acceptable salt or an in-vivo hydrolysable ester thereof.

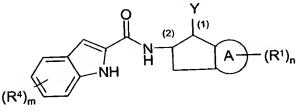
5. A compound of claim 1, wherein Y is OR^3, or a pharmaceutically acceptable salt or an in-vivo hydrolysable ester thereof.

6. A compound of claim 1, wherein m is 1 and R^4 is chlorine, or a pharmaceutically acceptable salt or an in-vivo hydrolysable ester thereof.

7. A compound of claim 1, wherein A is phenylene, or a pharmaceutically acceptable salt or an in-vivo hydrolysable ester thereof.

8. A compound of claim 1, wherein A is heteroarylene, or a pharmaceutically acceptable salt or an in-vivo hydrolysable ester thereof.

9. A compound of claim 1, which is a compound of formula (1A):



(1A)

or a pharmaceutically acceptable salt or an in-vivo hydrolysable ester thereof.

10. A compound of claim 1, selected from:
5-chloro-2-[*N*-(1-hydroxyindan-2-yl)carbamoyl]indole;
5-chloro-*N*-{(1*R*,2*R*)-1-[(methylsulfonyl)amino]-2,3-dihydro-1*H*-inden-2-yl}-1*H*-indole-2-carboxamide;
N-{(1*R**, 2*R**)-1-[(2-carboxyacetyl)amino]-2,3-dihydro-1*H*-inden-2-yl]-5-chloroindole-2-carboxamide;
5-chloro-*N*-{(1*R*,2*R*)-1-[(3-methoxypropanoyl)amino]-2,3-dihydro-1*H*-inden-2-yl}-1*H*-indole-2-carboxamide;
N-[(1*R*,2*R*)-1-(acetylamino)-2,3-dihydro-1*H*-inden-2-yl]-5-chloro-1*H*-indole-2-carboxamide;
5-chloro-*N*-[(1*R*,2*R*)-1-(*tert*-butoxycarbonylaminoacetamido)-2,3-dihydro-1*H*-inden-2-yl]-1*H*-indole-2-carboxamide;
N-((1*R*,2*R*)-1-{[3-(*tert*-butoxycarbonylamino)-4-oxopentanoyl]amino}-2,3-dihydro-1*H*-inden-2-yl)-5-chloro-1*H*-indole-2-carboxamide;
N-{(1*R*,2*R*)-1-[(2-carbamoylacetyl)amino]-2,3-dihydro-1*H*-inden-2-yl}-5-chloroindole-2-carboxamide;
N-{(1*R*,2*R*)-1-[(2-carboxyacetyl)amino]-2,3-dihydro-1*H*-inden-2-yl}-5-chloroindole-2-carboxamide;

5-chloro-*N*-{(1*R*,2*R*)-1-[(hydroxyacetyl)amino]-2,3-dihydro-1*H*-inden-2-yl}-1*H*-indole-2-carboxamide;

2-chloro-*N*-((1*R*,2*R*)-1-{[3-hydroxy-2-(hydroxymethyl)propanoyl]amino}-2,3-dihydro-1*H*-inden-2-yl)-1*H*-indole-2-carboxamide;

N-{(1*R*,2*R*)-1-[((3*R*)-3-amino-3-carbamoylpropanoyl)amino]-2,3-dihydro-1*H*-inden-2-yl}-5-chloroindole-2-carboxamide;

N-{(1*R*,2*R*)-1-[(aminoacetyl)amino]-2,3-dihydro-1*H*-inden-2-yl}-5-chloro-1*H*-indole-2-carboxamide;

5-chloro-*N*-{(1*S*,2*S*)-1-[(methylsulfonyl)amino]-2,3-dihydro-1*H*-inden-2-yl}-1*H*-indole-2-carboxamide;

5-chloro-*N*-{1-[(hydroxyacetyl)amino]-2,3-dihydro-1*H*-inden-2-yl}-1*H*-indole-2-carboxamide;

5-chloro-*N*-[(1*R*,2*R*)-1-({[(2-hydroxyethyl)(methyl)amino]acetyl}amino)-2,3-dihydro-1*H*-inden-2-yl]-1*H*-indole-2-carboxamide;

5-chloro-*N*-[(1*R*,2*R*)-1-({[(2-hydroxyethyl)(phenylmethyl)amino]acetyl} amino)-2,3-dihydro-1*H*-inden-2-yl]-1*H*-indole-2-carboxamide;

5-chloro-*N*-((1*R*,2*R*)-1-{[(3-hydroxypiperidin-1-yl)acetyl]amino}-2,3-dihydro-1*H*-inden-2-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-((1*R*,2*R*)-1-{[(3-hydroxypyrrolidin-1-yl)acetyl]amino}-2,3-dihydro-1*H*-inden-2-yl)-1*H*-indole-2-carboxamide;

N-[(1*R*,2*R*)-1-({[bis(2-hydroxyethyl)amino]acetyl}amino)-2,3-dihydro-1*H*-inden-2-yl]-5-chloro-1*H*-indole-2-carboxamide;

N-{1-[(aminoacetyl)amino]-2,3-dihydro-1*H*-inden-2-yl}-5-chloro-1*H*-indole-2-carboxamide;

N-{1-[((3*S*)-3-amino-3-carboxypropanoyl)amino]-2,3-dihydro-1*H*-inden-2-yl}-5-chloroindole-2-carboxamide;

5-chloro-*N*-((1*R*,2*R*)-1-{[(chloromethyl)sulfonyl]amino}-2,3-dihydro-1*H*-inden-2-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-(1-{[(trifluoromethyl)sulfonyl]amino}-2,3-dihydro-1*H*-inden-2-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-{1-[(cyanomethyl)amino]-2,3-dihydro-1*H*-inden-2-yl}-1*H*-indole-2-carboxamide;

5-chloro-*N*-{(1*R*,2*R*)-1-[(1*H*-tetrazol-5-ylmethyl)amino]-2,3-dihydro-1*H*-inden-2-yl}-1*H*-indole-2-carboxamide;

N-{(1*R*,2*R*)-1-[(2-amino-2-oxoethyl)amino]-2,3-dihydro-1*H*-inden-2-yl}-5-chloro-1*H*-indole-2-carboxamide;
N-[(1*R*,2*R*)-1-(carboxymethylamino)-2,3-dihydro-1*H*-inden-2-yl]-5-chloroindole-2-carboxamide;
N-{(1*S*,2*S*)-1-[acetyl(2-thienylmethyl)amino]-2,3-dihydro-1*H*-inden-2-yl}-5-chloro-1*H*-indole-2-carboxamide;
N-{(1*S*,2*S*)-1-[*N*-acetyl-*N*-(carboxymethyl)amino]-2,3-dihydro-1*H*-inden-2-yl}-5-chloroindole-2-carboxamide;
N-[(1*S*,2*S*)-1-{*N*-acetyl-*N*-[2-(ethoxycarbonyl)cycloprop-1ylmethyl]amino}-2,3-dihydro-1*H*-inden-2-yl]-5-chloroindole-2-carboxamide;
N-{(1*R*,2*R*)-1-[*N*-acetyl-*N*-(carboxymethyl)amino]-2,3-dihydro-1*H*-inden-2-yl}-5-chloroindole-2-carboxamide;
N-{(1*R*,2*R*)-1-[bis-(carboxymethyl)amino]-2,3-dihydro-1*H*-inden-2-yl}-5-chloroindole-2-carboxamide;
N-{(1*R*,2*R*)-1-[Acetyl(2-amino-2-oxoethyl)amino]-2,3-dihydro-1*H*-inden-2-yl}-5-chloro-1*H*-indole-2-carboxamide;
N-{(1*R*,2*R*)-1-[*N*-(2-acetoxyacetyl)-*N*-(carboxymethyl)amino]-2,3-dihydro-1*H*-inden-2-yl}-5-chloroindole-2-carboxamide;
5-chloro-*N*-[(1*R*,2*R*)-1-(2,5-dioxomorpholin-4-yl)-2,3-dihydro-1*H*-inden-2-yl]-1*H*-indole-2-carboxamide; and
5-chloro-*N*-((1*R*,2*R*)-1-{[(2*R*)-2,3-dihydroxypropyl]amino}-2,3-dihydro-1*H*-inden-2-yl)-1*H*-indole-2-carboxamide;
or a pharmaceutically acceptable salt or an in-vivo hydrolysable ester thereof.

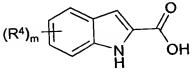
11. A pharmaceutical composition which comprises a compound of claim 1, or a pharmaceutically acceptable salt or in-vivo hydrolysable ester thereof in association with a pharmaceutically acceptable diluent or carrier.

12. A method for the treatment of type 2 diabetes, insulin resistance, syndrome X, hyperinsulinaemia, hyperglucagonaemia, cardiac ischaemia or obesity in a warm-blooded animal, comprising administering a compound of claim 1, or a pharmaceutically acceptable salt or in-vivo hydrolysable ester thereof.

13. A method for the treatment of type 2 diabetes in a warm-blooded animal, comprising administering a compound of claim 1, or a pharmaceutically acceptable salt or in-vivo hydrolysable ester thereof.

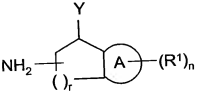
14. A process for the preparation of a compound of claim 1, which process comprises:

reacting an acid of the formula (2)



(2)

or an activated derivative thereof; with an amine of formula (3)



(3)

and thereafter if necessary

i) converting a compound of the formula (1) into another compound of the formula (1);

ii) removing any protecting groups; or

iii) forming a pharmaceutically acceptable salt or *in vivo* hydrolysable ester.